



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

SEP 25 1987

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Chlordimeform 6(a)(2) data notifications. Hoechst AG
Dye Plant Epidemiology Study. Accession No. 401583-01.
Caswell File #174A.

FROM: Stanley B. Gross, Ph.D., Toxicologist
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8/7/87

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THRU: Albin B. Kocialski, Ph.D., Supervisory Pharmacologist
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ABK 9/21/87

and

Theodore M. Farber, Ph.D., Chief
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Theodore M. Farber
9/25/87

Request:

Ciba-Geigy Corporation has submitted the following study report as 6(a)(2) data in its letter from Jerry Harrison and Paula F. Paul (Nor-Am Chemical Company) consisting of:

A one-page of summary statement by Mirosław Jan Stasik (Technical University of Munich) of his study previously submitted to the Agency: "A historic Cohort Study of 4-chloro-2-methylaniline Workers." Stasik, M.J., Lange, H. -J.; Ulm, K. and Schuckmann, F. Department of Occupational Medicine, Hoechst AG, Frankfurt and Department of Epidemiology, Technical University of Munich.

Historical Comments

A manuscript for publication of this study was submitted to the Agency by Ciba-Geigy on September 17, 1986. This cancer epidemiology study concerns worker exposure to 4-chloro-o-toluidine (also known as 5-CAT). 5-CAT is of concern to the Agency as TSCA 8(e) data and to Pesticides as 6(a)(2) data because 5-CAT is one of the metabolites of Chlordimeform, currently under special review.

This study was sent for review to Toxicology Branch by Special Review Branch. Toxicology's review was sent to Special Review Branch on April 28, 1987 (Memorandum to W. Waldrop/D. McKinney from S. Gross, attached) indicating the need to have a number of questions about the study answered by Hoechst. A number of these concerns were discussed at a meeting on 4/29/87 (see listing of questions by S. Gross, attached) with EPA staff from Toxics and Pesticides and Dr. Heinz Trebitz (American Hoechst, New Jersey) and Dr. Fritz Schuckman (Hoechst, Frankfurt), one of the investigator/pathologists who worked on the dye plant study. These concerns were later summarized in a May 29, 1987 memorandum by Gary Burin to Jan Auebach (attached).

Dr. Schuckman had indicated in the 4/29/87 meeting at EPA, that Hoechst would provide additional information on the study as requested. Thus far, the Agency has received pathological detail on the 8 bladder cancers found in the study sent in a letter of May 1, 1987 from Dr. Trebitz.

Summary of Dye Worker Study.

Three hundred thirty five male workers who had worked in the Hoechst dye plant in Germany from 1929 to 1982 were evaluated. The workers in the study were said to have been exposed to 5-CAT (4-chloro-2-methyl aniline) for at least 12 months. There were not data presented which attempted to quantitate the type and amount of exposure to the workers. Of the 335 workers, 5 of them developed cancer of the stomach, prostate and brain. The overall tumor rates were approximately normal, however, the brain tumors (observed in 2 workers) was considered higher than expected.

Toxicology Branch concluded: 1) Documentation for the bladder cancers in the Hoechst plant has not been provided. 2) There remained a question of the actual exposures in these workers relative to the chemicals involved and the amount of exposure. 3) Therefore the results of this investigation impacts on the Special Review process only to the extent that these questions are unanswered.

Conclusions

The present submission does not contribute any additional information beyond that which was previously submitted.

A number of issues remain concerning the Hoechst dye plant epidemiology study. Most importantly is information on possible exposures to multiple other chemicals capable of causing tumor as well as some objective measures of worker exposures.

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